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| 10/561,951 | 11/21/2006 | **Yannick Guilloux** | 283632US0XPCT | 8052 |

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| EXAMINER | |
|---|---|
| DUFFY, BRADLEY | |
| **ART UNIT** | **PAPER NUMBER** |
| 1643 | |

| NOTIFICATION DATE | DELIVERY MODE |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/561,951 | GUILLOUX ET AL. | |
| | Examiner | Art Unit | |
| | BRAD DUFFY | 1643 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The preliminary amendment filed December 22, 2005 is acknowledged and has been entered. Claims 1-13 have been amended. Claims 14-19 have been newly added.

2. Claims 1-19 are pending in this application and are currently subject to restriction.

### *Election/Restrictions*

3. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1 and 14, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a MMP-2 metalloprotease to the patient.

Group II, claims 1, 6, 7, and 14-16, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

Group III, claims 1 and 14, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a MHC I presented fragment of a MMP-2 metalloprotease comprising a T epitope to

the patient.

Group VI, claims 1 and 14, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a MHC II presented fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

Group V, claims 1 and 14, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a polynucleotide encoding a MMP-2 metalloprotease to the patient.

Group VI, claims 1 and 14, insofar as the claims are drawn to a method of treating cancer in a patient in need thereof comprising administering an effective amount of a polynucleotide encoding a fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

Group VII to Group LXVII, claims 1 and 14, insofar as the claims are drawn to a treating cancer in a patient by administering one specific combination[1] of compounds to the patient, wherein the compounds are selected from the group consisting of: a MMP-2 metalloprotease; a fragment of a MMP-2 metalloprotease comprising a T epitope; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC I; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC II; a polynucleotide encoding a MMP-2 metalloprotease; a polynucleotide encoding a fragment of a MMP-2 metalloprotease comprising a T epitope.

[1] In this case there are 57 different combinations of the 6 compounds recited in claim 1, i.e., 15 combinations wherein 2 compounds are administered, 20 combinations wherein 3 compounds are administered, 15 combinations wherein 4 compounds are administered, 6 combinations wherein 5 compounds are administered and 1 combination wherein all 6 compounds are administered. Accordingly, there are 57 different Groups that correspond to each specific combination of compounds. Therefore, if Applicant elects any one of Group VII to Group LXVII, Applicant is required to set forth the one specific combination of compounds that corresponds to the elected Group

Group LXVIII, claims 2, 3, 5 and 13, drawn to a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease and compositions comprising such a peptide and an adjuvant.

Group LXIX, claims 4, 17 and 19, drawn to a polynucleotide that encodes a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease and compositions comprising such a polynucleotide and an adjuvant.

Group LXX, claims 8 and 18, drawn to isolated antigen-presenting cells expressing an MHC I molecule, wherein the isolated antigen-presenting cell is loaded, in vitro, with a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

Group LXXI, claims 9 and 10, drawn to isolated antigen-presenting cells expressing an MHC I molecule, wherein the isolated antigen-presenting cell is transfected with a polynucleotide that encodes a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

Group LXXII, claim 11, insofar as the claim is drawn to a method of preparing cytotoxic T lymphocytes directed against the MMP-2 metalloprotease, comprising selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma those cytotoxic T lymphocytes that recognize the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

Group LXXIII, claim 11, insofar as the claim is drawn to a method of preparing cytotoxic T lymphocytes directed against the MMP-2 metalloprotease, comprising selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize a fragment of the MMP-2

protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

Group LXXIV, claim 12, insofar as the claim is drawn to a preparation of cytotoxic T lymphocytes directed against the MMP-2 metalloprotease prepared by selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

Group LXXV, claim 12, insofar as the claim is drawn to a preparation of cytotoxic T lymphocytes directed against the MMP-2 metalloprotease prepared by selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize a fragment of the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

4. The inventions listed as Groups I-LXXV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

To have a general inventive concept under PCT Rule 13.1, the inventions need to be linked by a special technical feature. The technical feature recited in claim 1 is treating cancer in a patient by administering at least one compound to the patient, wherein the at least one compound is selected from the group consisting of: a MMP-2 metalloprotease; a fragment of a MMP-2 metalloprotease comprising a T epitope; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC I; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC II; a polynucleotide encoding a MMP-2 metalloprotease; a polynucleotide encoding a fragment of a MMP-2 metalloprotease comprising a T epitope; and combinations thereof. This claim lacks an inventive step over WO/2002/098351 (Brooks et al, 2002,

cited by Applicant; IDS filed 3/14/2006). Brooks et al teach methods of treating cancer in a patient comprising administering a MMP-2 metalloprotease to the patient or administering a fragment of a MMP-2 metalloprotease to a patient (see entire document, e.g., page 3 and 4). Since Brooks et al teach the technical feature recited in claim 1, it is not a special technical feature and the groups do not relate to a single general inventive concept as required under PCT Rule 13.1. Furthermore, PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept to comprise more than the first mentioned product, the first mentioned method for making said product, and the first mentioned method for using said product.

For these reasons, the special technical feature of the invention of Group I is treating cancer in a patient comprising administering an effective amount of a MMP-2 metalloprotease to the patient.

The special technical feature of the invention of Group II is treating cancer in a patient comprising administering an effective amount of a fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

The special technical feature of the invention of Group III is treating cancer in a patient comprising administering an effective amount of a MHC I presented fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

The special technical feature of the invention of Group VI is treating cancer in a patient comprising administering an effective amount of a MHC II presented fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

The special technical feature of the invention of Group V is treating cancer in a patient comprising administering an effective amount of a polynucleotide encoding a MMP-2 metalloprotease to the patient.

The special technical feature of the invention of Group VI is treating cancer in a patient comprising administering an effective amount of a polynucleotide encoding a fragment of a MMP-2 metalloprotease comprising a T epitope to the patient.

The special technical feature of the inventions of Groups VII-LXVII is treating cancer in a patient by administering the one specific combination[2] of compounds which corresponds to each different group, respectively, to the patient, wherein the compounds are selected from the group consisting of: a MMP-2 metalloprotease; a fragment of a MMP-2 metalloprotease comprising a T epitope; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC I; a fragment of a MMP-2 metalloprotease comprising a T epitope presented by MHC II; a polynucleotide encoding a MMP-2 metalloprotease; a polynucleotide encoding a fragment of a MMP-2 metalloprotease comprising a T epitope.

The special technical feature of the invention of Group LXVIII is a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

The special technical feature of the invention of Group LXIX is a polynucleotide that encodes a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

The special technical feature of the invention of Group LXX is antigen-presenting cells expressing an MHC I molecule, wherein the isolated antigen-presenting cell is loaded, in vitro, with a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

The special technical feature of the invention of Group LXXI is antigen-presenting

[2] As set forth above there are 57 different combinations of the 6 compounds which are administered to patients to treat cancer. Accordingly, administering one specific combination to treat cancer is considered the special technical feature of each single group of Groups VII-LXVII, respectively.

cells expressing an MHC I molecule, wherein the isolated antigen-presenting cell is transfected with a polynucleotide that encodes a peptide that comprises a fragment of 8-11 consecutive amino acids of the MMP-2 metalloprotease.

The special technical feature of the invention of Group LXXII is preparing cytotoxic T lymphocytes directed against the MMP-2 metalloprotease, comprising selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma those cytotoxic T lymphocytes that recognize the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

The special technical feature of the invention of Group LXXIII is preparing cytotoxic T lymphocytes directed against the MMP-2 metalloprotease, comprising selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize a fragment of the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

The special technical feature of the invention of Group LXXIV is a preparation of cytotoxic T lymphocytes directed against the MMP-2 metalloprotease prepared by selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

The special technical feature of the invention of Group LXXV is a preparation of cytotoxic T lymphocytes directed against the MMP-2 metalloprotease prepared by selecting from cytotoxic T lymphocytes taken from a patient suffering from melanoma, those cytotoxic T lymphocytes that recognize a fragment of the MMP-2 protein and the multiplying, in vitro, the selected T lymphocytes thus selected.

Accordingly the groups are not so linked as to form a single general concept under PCT Rule 13.1.

5. **Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.** The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116;

amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached at Monday through Friday from 7:00 AM to 4:30 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are

unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
March 24, 2008